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(54) Title: COSMETIC COMPOSITIONS WITH AMMONIUM MALONATES

(57) Abstract: A cosmetic composition is provided which includes as an active material a salt formed from neutralization of malonic acid with ammonia or a C1-C10 hydrocarbyl amine, the composition having a pH from 1.8 to 6.5. Particularly preferred is ammonium malonate.

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COSMETIC COMPOSITIONS WITH AMMONIUM MALONATES

The invention concerns cosmetic compositions containing ammonium malonates which combat the signs of skin aging.

5

A soft, supple and flexible skin has a marked cosmetic appeal, and is an attribute of normal functioning epidermis. As human skin ages with advancing years, the epidermis can become folded, ridged or furrowed to form wrinkles. These  
10 signal loss of youthful appearance and herald the transition to old age. Exposure to excessive doses of sunlight accelerates the transition process. Also, the outer layer of the epidermis known as the stratum corneum can become dry and flaky following exposure to cold weather or excessive  
15 contact with detergents or solvents. Loss of skin moisture thereby results, and the skin begins to lose the soft, supple and flexible characteristics.

Emollients such as fats, phospholipids and sterols have in the past been used to soften wrinkled or dry skin. These  
20 emollients are only partially effective as a remedy for skin in poor condition.

The use of hydroxy carboxylic acids for enhancing the quality of human skin has been known for some time. There is no doubt that alpha-hydroxy carboxylic acids are  
25 effective much beyond the common emollients.

U.S. Patent 4,424,234 (Alderson et al.) discloses skin treatment compositions incorporating alpha-hydroxycaproic

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acid and alpha-hydroxycaprylic acid or mixtures thereof in compositions that have a pH value of less than 7, usually from 2 to 4. Yu and Van Scott have patented widely in this area. For instance, U.S. Patent 4,105,782 reports amines or  
5 ammonium salts of alpha-hydroxy carboxylic acids in the treatment of acne or dandruff. In U.S. Patent 4,105,783 and U.S. Patent 4,197,316, these compounds are suggested for the treatment of dry skin. U.S. Patent 4,234,599 discloses the use of alpha-hydroxy carboxylic acids, their esters or amine  
10 salts in the treatment of keratoses. More recently, U.S. Patent 5,091,171 focused attention on these compounds as being effective against age spots, wrinkles and aging related skin changes.

While hydroxy carboxylic acids hold much therapeutic  
15 promise, the materials have been found to irritate human skin on repeated topical applications. The irritation may range from a sensation of tingling, itching and burning to clinical signs of redness and peeling. Causes for such irritation have been linked to the lowering of pH in the  
20 stratum corneum of human skin. Low pH has been suggested as provoking disturbances in intercorneocyte bondings resulting in adverse skin reactions, specially in some individuals with sensitive skin.

Organic acids other than alpha-hydroxy functionalized have  
25 been disclosed in the cosmetic literature. For instance, U.S. Patent 5,641,495 (Jokura et al.) discloses in combination a ceramide or pseudoceramide, a dicarboxylic acid and a salt of a dicarboxylic acid. The examples illustrate sodium and potassium salts of succinic acid.

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Lower molecular weight dicarboxylic acids such as malonic may also be utilized.

Although excellent moisturization and little accompanying irritation occurs, there is no suggestion that this system  
5 combats signs of aging such as advent of fine lines and wrinkles. Improvements in the general anti-ageing technology of skin remains as an unfulfilled need of the consumer.

Accordingly, it is an advantage of the present invention to  
10 be able to provide new cosmetic ingredients in compositions which are effective at controlling and even eliminating the signs of aging, particularly fine lines, wrinkles, sagging skin, poor tone and age spots.

In a first aspect of the invention, there is provided a  
15 cosmetic composition which includes:

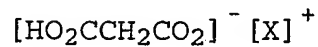
- (i) from about 0.0001% to about 30% by weight of a salt which is an amine neutralized malonic acid;
- (ii) from about 1% to about 99.9% by weight of a cosmetically acceptable carrier;

20 wherein the composition has a pH ranging from about 1.8 to 6.5.

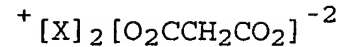
We have now found a class of salts which are at least as effective as alpha-hydroxy carboxylic acids. These salts are based on malonic acid neutralized with an amine which is  
25 ammonia or a C<sub>1</sub>-C<sub>10</sub> hydrocarbyl amine as the active salt ingredient. These salts may either be the half or fully

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neutralized malonate salts or combinations thereof as represented by general formulas (I) and (II):



I



II

5 wherein X is a protonated ammonia or a C<sub>1</sub>-C<sub>10</sub> hydrocarbyl amine.

Illustrative amines include ammonia, triethanolamine, diethanolamine, monoethanolamine, methylamine, ethylamine, propylamine, isopropylamine, butylamine, isobutylamine, t-  
10 butylamine, pentylamine, isopentylamine, hexylamine, cyclohexylamine, cyclopentylamine, norbornylamine, octylamine, ethylhexylamine, nonylamine, decylamine and combinations thereof. Most preferred is ammonia which forms the ammonium salts of malonate and includes ammonium malonate  
15 and diammonium malonate.

Amounts of the amine neutralized malonic acid salt may range from about 0.0001% to about 30%, preferably from about 0.1% to about 15%, more preferably from about 0.5% to about 10%, optimally from about 1% to about 8% by weight of the  
20 cosmetic composition.

The present invention can utilize as the active ingredient salt I, salt II or mixtures of these salts. When mixtures are present the molar ratio of mono-salt I to di-salt II may range from about 1000:1 to about 1:1000, preferably from

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about 10:1 to about 1:500, more preferably from about 2:1 to about 1:200, optimally from about 1:1 to about 1:20.

Compositions of this invention may have a pH ranging from about 1.8 to about 6.5, preferably from about 2.5 to about 6, optimally from about 3 to about 5.5, more optimally from about 3.5 to about 4.5.

Compositions of this invention will also include a cosmetically acceptable carrier. Amounts of the carrier may range from 1% to 99.9%, preferably from about 70% to about 95%, optimally from about 80% to about 90%. Among the useful carriers are water, emollients, fatty acids, fatty alcohols, humectants, thickeners and combinations thereof. The carrier may be aqueous, anhydrous or an emulsion. Preferably the compositions are aqueous, especially water and oil emulsions of the W/O or O/W variety. Water when present may be in amounts ranging from about 5% to about 95%, preferably from about 20% to about 70%, optimally from about 35% to about 60% by weight.

Emollient materials may serve as cosmetically acceptable carriers. These may be in the form of silicone oils, synthetic esters and hydrocarbons. Amounts of the emollients may range anywhere from about 0.1% to about 95%, preferably between about 1% and about 50% by weight.

Silicone oils may be divided into the volatile and non-volatile variety. The term "volatile" as used herein refers to those materials which have a measurable vapor pressure at ambient temperature. Volatile silicone oils are preferably

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chosen from cyclic (cyclomethicone) or linear polydimethylsiloxanes containing from 3 to 9, preferably from 4 to 5, silicon atoms.

Non-volatile silicone oils useful as an emollient material  
5 include polyalkyl siloxanes, polyalkylaryl siloxanes and polyether siloxane copolymers. The essentially nonvolatile polyalkyl siloxanes useful herein include, for example, polydimethyl siloxanes with viscosities of from about  $5 \times 10^{-6}$  to  $0.1 \text{ m}^2/\text{s}$  at  $25^\circ\text{C}$ . Among the preferred non-volatile  
10 emollients useful in the present compositions are the polydimethyl siloxanes having viscosities from about  $1 \times 10^{-5}$  to about  $4 \times 10^{-4} \text{ m}^2/\text{s}$  at  $25^\circ\text{C}$ .

Another class of non-volatile silicones are emulsifying and non-emulsifying silicone elastomers. Representative of this  
15 category is Dimethicone/Vinyl Dimethicone Crosspolymer available as Dow Corning 9040, General Electric SFE 839, and Shin-Etsu KSG-18. Silicone waxes such as Silwax WS-L (Dimethicone Copolyol Laurate) may also be useful.

Among the suitable ester emollients are:

- 20 (1) Alkenyl or alkyl esters of fatty acids having 10 to 20 carbon atoms. Examples thereof include isoarachidyl neopentanoate, isononyl isonanonoate, oleyl myristate, oleyl stearate, and oleyl oleate.
- (2) Ether-esters such as fatty acid esters of ethoxylated  
25 fatty alcohols.

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- 5 (3) Polyhydric alcohol esters. Ethylene glycol mono and di-fatty acid esters, diethylene glycol mono- and di-fatty acid esters, polyethylene glycol (200-6000) mono- and di-fatty acid esters, propylene glycol mono- and di-fatty acid esters, polypropylene glycol 2000 monooleate, polypropylene glycol 2000 monostearate, ethoxylated propylene glycol monostearate, glyceryl mono- and di-fatty acid esters, polyglycerol poly-fatty esters, ethoxylated glyceryl mono-stearate, 1,3-butylene glycol monostearate, 1,3-butylene glycol distearate, polyoxyethylene polyol fatty acid ester, sorbitan fatty acid esters, and polyoxyethylene sorbitan fatty acid esters are satisfactory polyhydric alcohol esters. Particularly useful are pentaerythritol, trimethylolpropane and neopentyl glycol esters of C<sub>1</sub>-C<sub>30</sub> alcohols.
- 10
- 15
- (4) Wax esters such as beeswax, spermaceti wax and tribehenin wax.
- 20 (5) Sterols esters, of which cholesterol fatty acid esters are examples thereof.
- (6) Sugar ester of fatty acids such as sucrose polybehenate and sucrose polycottonseedate.

Hydrocarbons which are suitable cosmetically acceptable  
25 carriers include petrolatum, mineral oil, C<sub>11</sub>-C<sub>13</sub> isoparaffins, polyalphaolefins, and especially



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isohexadecane, available commercially as Permethyl 101A from Presperse Inc.

Fatty acids having from 10 to 30 carbon atoms may also be suitable as cosmetically acceptable carriers. Illustrative  
5 of this category are pelargonic, lauric, myristic, palmitic, stearic, isostearic, hydroxystearic, oleic, linoleic, ricinoleic, arachidic, behenic and erucic acids.

Fatty alcohols having from 10 to 30 carbon atoms are another useful category of cosmetically acceptable carrier.  
10 Illustrative of this category are stearyl alcohol, lauryl alcohol, myristyl alcohol and cetyl alcohol.

Humectants of the polyhydric alcohol-type can be employed as cosmetically acceptable carriers. Typical polyhydric alcohols include glycerol, polyalkylene glycols and more  
15 preferably alkylene polyols and their derivatives, including propylene glycol, dipropylene glycol, polypropylene glycol, polyethylene glycol and derivatives thereof, sorbitol, hydroxypropyl sorbitol, hexylene glycol, 1,3-butyleneglycol, isoprene glycol, 1,2,6-hexanetriol, ethoxylated  
20 glycerol, propoxylated glycerol and mixtures thereof. The amount of humectant may range anywhere from 0.5% to 50%, preferably between 1% and 15% by weight of the composition.

Thickeners can be utilized as part of the cosmetically acceptable carrier of compositions according to the present  
25 invention. Typical thickeners include crosslinked acrylates (e.g. Carbopol 982®), hydrophobically-modified acrylates (e.g. Carbopol 1382®), cellulosic derivatives and natural

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gums. Among useful cellulosic derivatives are sodium carboxymethylcellulose, hydroxypropyl methocellulose, hydroxypropyl cellulose, hydroxyethyl cellulose, ethyl cellulose and hydroxymethyl cellulose. Natural gums  
5 suitable for the present invention include guar, xanthan, sclerotium, carrageenan, pectin and combinations of these gums. Inorganics may also be utilized as thickeners, particularly clays such as bentonites and hectorites, fumed silicas, and silicates such as magnesium aluminum silicate  
10 (Veegum®). Amounts of the thickener may range from 0.0001% to 10%, usually from 0.001% to 1%, optimally from 0.01% to 0.5% by weight.

Cosmetic compositions of the present invention may be in any form. These forms may include lotions, creams, roll-on  
15 formulations, sticks, mousses, aerosol and non-aerosol sprays and pad-applied formulations.

Surfactants may also be present in cosmetic compositions of the present invention. Total concentration of the surfactant when present may range from about 0.1% to about  
20 40%, preferably from about 1% to about 20%, optimally from about 1% to about 5% by weight of the composition. The surfactant may be selected from the group consisting of anionic, nonionic, cationic and amphoteric actives.

Particularly preferred nonionic surfactants are those with a  
25 C<sub>10</sub>-C<sub>20</sub> fatty alcohol or acid hydrophobe condensed with from 2 to 100 moles of ethylene oxide or propylene oxide per mole of hydrophobe; C<sub>2</sub>-C<sub>10</sub> alkyl phenols condensed with from 2 to

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20 moles of alkylene oxide; mono- and di-fatty acid esters of ethylene glycol; fatty acid monoglyceride; sorbitan, mono- and di- C<sub>8</sub>-C<sub>20</sub> fatty acids; and polyoxyethylene sorbitan as well as combinations thereof. Alkyl  
5 polyglycosides and saccharide fatty amides (e.g. methyl gluconamides) are also suitable nonionic surfactants.

Preferred anionic surfactants include soap, alkyl ether sulfates and sulfonates, alkyl sulfates and sulfonates, alkylbenzene sulfonates, alkyl and dialkyl sulfosuccinates,  
10 C<sub>8</sub>-C<sub>20</sub> acyl isethionate, C<sub>8</sub>-C<sub>20</sub> alkyl ether phosphates, C<sub>8</sub>-C<sub>20</sub> sarcosinates and combinations thereof.

Sunscreen actives may also be included in compositions of the present invention. Particularly preferred are such materials as ethylhexyl p-methoxycinnamate, available as  
15 Parsol MCX®, Avobenzene, available as Parsol 1789® and benzophenone-3, also known as Oxybenzone. Inorganic sunscreen actives may be employed such as microfine titanium dioxide, zinc oxide, polyethylene and various other polymers. Amounts of the sunscreen agents when present may  
20 generally range from 0.1% to 30%, preferably from 2% to 20%, optimally from 4% to 10% by weight.

Preservatives can desirably be incorporated into the cosmetic compositions of this invention to protect against the growth of potentially harmful microorganisms. Suitable  
25 traditional preservatives for compositions of this invention are alkyl esters of para-hydroxybenzoic acid. Other preservatives which have more recently come into use include

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hydantoin derivatives, propionate salts, and a variety of quaternary ammonium compounds. Cosmetic chemists are familiar with appropriate preservatives and routinely choose them to satisfy the preservative challenge test and to provide product stability. Particularly preferred preservatives are phenoxyethanol, methyl paraben, propyl paraben, imidazolidinyl urea, sodium dehydroacetate and benzyl alcohol. The preservatives should be selected having regard for the use of the composition and possible incompatibilities between the preservatives and other ingredients in the emulsion. Preservatives are preferably employed in amounts ranging from 0.01% to 2% by weight of the composition.

Compositions of the present invention may include vitamins. Illustrative vitamins are Vitamin A (retinol), Vitamin B<sub>2</sub>, Vitamin B<sub>6</sub>, Vitamin C, Vitamin E and Biotin. Derivatives of the vitamins may also be employed. For instance, Vitamin C derivatives include ascorbyl tetraisoalmitate, magnesium ascorbyl phosphate and ascorbyl glycoside. Derivatives of Vitamin E include tocopheryl acetate, tocopheryl palmitate and tocopheryl linoleate. DL-panthenol and derivatives may also be employed. Total amount of vitamins when present in compositions according to the present invention may range from 0.001% to 10%, preferably from 0.01% to 1%, optimally from 0.1% to 0.5% by weight.

Another type of useful substance can be that of an enzyme such as oxidases, proteases, lipases and combinations.

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Particularly preferred is superoxide dismutase, commercially available as Biocell SOD from the Brooks Company, USA.

Skin lightening compounds may be included in the compositions of the invention. Illustrative substances are placental extract, lactic acid, niacinamide, arbutin, kojic acid, ferulic acid, resorcinol and derivatives including 4-substituted resorcinols and combinations thereof. Amounts of these agents may range from about 0.1% to about 10%, preferably from about 0.5% to about 2% by weight of the compositions.

Desquamation promoters may be present. Illustrative are the alpha-hydroxycarboxylic acids and beta-hydroxycarboxylic acids. The term "acid" is meant to include not only the free acid but also salts and C<sub>1</sub>-C<sub>30</sub> alkyl or aryl esters thereof and lactones generated from removal of water to form cyclic or linear lactone structures. Representative acids are glycolic, lactic and malic acids. Salicylic acid is representative of the beta-hydroxycarboxylic acids. Amounts of these materials when present may range from about 0.1% to about 15% by weight of the composition.

A variety of herbal extracts may optionally be included in compositions of this invention. Illustrative are green tea, chamomile, licorice and extract combinations thereof. The extracts may either be water soluble or water-insoluble carried in a solvent which respectively is hydrophilic or hydrophobic. Water and ethanol are the preferred extract solvents.

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Also included may be such materials as lipoic acid, retinoyxytrimethylsilane (available from Clariant Corp. under the Silcare 1M-75 trademark), ceramides (including Ceramide 1, Ceramide 3, Ceramide 3B and Ceramide 6),  
5 dehydroepiandrosterone (DHEA) and combinations thereof. Amounts of these materials may range from about 0.000001% to about 10%, preferably from about 0.0001% to about 1% by weight.

10 Colorants, fragrances, opacifiers and abrasives may also be included in compositions of the present invention. Each of these substances may range from about 0.05% to about 5%, preferably between 0.1% and 3% by weight.

The term "comprising" is meant not to be limiting to any subsequently stated elements but rather to encompass non-  
15 specified elements of major or minor functional importance. In other words the listed steps, elements or options need not be exhaustive. Whenever the words "including" or "having" are used, these terms are meant to be equivalent to "comprising" as defined above.

20 Except in the operating and comparative examples, or where otherwise explicitly indicated, all numbers in this description indicating amounts of material ought to be understood as modified by the word "about".

#### Examples

25 The following examples will more fully illustrate the embodiments of this invention. All parts, percentages and

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proportions referred to herein and in the appended claims are by weight unless otherwise illustrated.

Example 1

5

A clinical study was conducted to compare ammonium malonate to ammonium glycolate as active cosmetic ingredients. The base formula for the comparative experiments is outlined under Table I.

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TABLE I

INGREDIENT	WEIGHT %
PHASE A	
Water	Balance
Disodium EDTA	0.05
Methyl Paraben	0.15
Magnesium Aluminum Silicate	0.60
Triethanolamine	1.20
PHASE B	
Xanthan Gum	0.20
Natrosol® 250HHR (ethyl cellulose)	0.50
Butylene Glycol	3.00
Glycerin	2.00
PHASE C	
Sodium Stearoyl Lactylate	0.10
Glycerol Monostearate	1.50
Stearyl Alcohol	1.50
Isostearyl Palmitate	3.00
Silicone Fluid	1.00
Cholesterol	0.25
Sorbitan Stearate	1.00
Butylated Hydroxy Toluene	0.05
Vitamin E Acetate	0.01
PEG-100 Stearate	2.00
Stearic Acid	3.00
Propyl Paraben	0.10
Parsol MCX®	2.00
Caprylic/Capric Triglyceride	0.50
Hydroxycaprylic Acid	0.01
C12-15 Alkyl Octanoate	3.00
PHASE D	
Active	-
PHASE E	
Vitamin A Palmitate	0.10
Bisabolol	0.01
Vitamin A Acetate	0.01
Fragrance	0.03
Retinol 50C	0.02



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The total formulations with ammonium glycolate and ammonium malonate active are identified in the Tables below as "PADC" and "Ammonium". The PADC product is a state of the art alpha hydroxy acid formula which is currently in the market. This  
5 formula contains 8% Glycolic acid or 0.1053 equivalents, neutralized with 2.4% ammonia hydroxide which is 0.0395 equivalents, resulting in a final formula pH of 3.8. The ammonium formula contains 5.04% malonic acid or 0.0969  
10 equivalents, neutralized with 1.87% ammonia which is 0.0311 equivalents, resulting in a final formula pH of 3.6-4.0. This resulted in Malonic acid being 31.87% neutralized by the amine.

The clinical involved 49 panellists over asix week period. Panellists were required to apply each product to one half of  
15 their face. After application, the panellists were required to answer a series of questions regarding relative effectiveness of the products.

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TABLE II

Products:	Week 1 (n=49)			Week 3 (n=49)			Week 6 (n=47)		
PADC & Ammonium Malonate pH 3.6-4.0	PADC	Ammonium	no pref	PADC	Ammonium	no pref	PADC	Ammonium	No pref
Absorbed more easily	31	39	30	35	29	37	30	23	47
Felt less greasy	26	43	31	31	33	37	30	30	40
Felt lighter	33	39	28	35	35	31	32	34	34
Left skin feeling softer	24	22	54	29	18	53	30	15	55
Was milder	20	37	43	29	20	51	28	26	45
Left skin feeling smoother	24	22	54	29	12	59	32	13	55
Left skin looking smoother	22	15	63	27	14	59	28	19	53
Moisturized better	28	26	46	33	14	53	21	13	66
Helped to look firmer/tighter	26	22	52	22	16	61	26	15	59
Helped to feel healthier	19	13	69	22	10	67	23	13	64
Helped to feel firmer/tighter	24	24	52	22	25	53	25	19	57
Improved skin tone better	20	11	69	22	12	65	24	17	59
Made skin look better	20	17	63	25	10	65	25	13	62
Improved condition better	20	19	61	20	16	63	28	15	57
Helped to look younger	20	13	67	20	14	65	23	11	66
Left skin more radiant	17	17	67	14	12	74	13	15	72
Was less irritating	23	36	41	26	25	49	28	30	42
Was evening out tone/texture	15	9	76	18	10	71	21	9	70
Firmed skin better	24	19	57	20	20	59	28	19	53

## Overall preference

Products:	Week 1			Week 3			Week 6		
PADC & Ammonium Malonate pH 3.6-4.0	PADC	Ammonium	no pref	PADC	Ammonium	no pref	PADC	Ammonium	No pref
Overall Preference	41	33	26	35	37	29	36	34	30

5

Based on the results of the clinical evaluations, it is evident that ammonium malonate is nearly as effective as ammonium glycolate, the well-known, but irritation inducing active, in respect of improving the general condition of skin.

10

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Additionally, a further more extensive clinical found that ammonium malonate was considerably less irritating than the ammonium glycolate composition. Results of that study are summarized in the Table below. The products evaluated  
5 herein were identical to those fielded in the first clinical study.

Overall Skin Problems Experienced

Products	Week 1		Week 4		Week 8	
	PADC	Ammon. Malonate	PADC	Ammon. Malonate	PADC	Ammon. Malonate
Yes	24%	11%	10%	5%	9%	5%
No	76%	89%	90%	95%	91%	95%

10 The types of skin problems experienced that were recorded included any redness/splotches, pimples/breakouts/acne, tingling, burning, dryness, stinging, itching, irritation/discomfort, bumps, rash, peeling, puffiness, flaking, tightness, blotchiness, blisters/blistering and any  
15 other similar manifestation. Approximately 100 panellists were used in this clinical. It is evident that in the first week of use, the ammonium malonate is much less discomforting to the face than the ammonium glycolate. After several weeks of use, the panellists became acclimated  
20 and the difference between the materials became less although still discernible.

#### Example 2

25 A water-in-oil topical liquid make-up foundation utilizing the malonate salts of the present invention is described in Table IV below.

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TABLE IV

INGREDIENT	WEIGHT %
PHASE A	
Cyclomethicone	9.25
Cetyl Octanoate	2.00
Dimethicone Copolyol	20.00
PHASE B	
Talc	3.38
Pigment (Iron Oxides)	10.51
Spheron L-1500 (Silica)	0.50
PHASE C	
Synthetic Wax Durachem 0602	0.10
Arachidyl Behenate	0.30
PHASE D	
Cyclomethicone	1.00
Trihydroxystearin	0.30
PHASE E	
Laureth-7	0.50
Propyl Paraben	0.25
PHASE F	
Fragrance	0.05
PHASE G	
Water	balance
Ammonium Malonate	3.00
Methyl Paraben	0.12
Propylene Glycol	8.00
Niacinamide	4.00
Glycerin	3.00
Sodium Chloride	2.00
Sodium Dehydroacetate	0.30

5 Example 3

Illustrated herein is a skin cream incorporating the malonate salts of the present invention.

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TABLE V

INGREDIENT	WEIGHT %
Glycerin	6.93
Niacinamide	5.00
Ammonium Malonate	5.00
Permethyl 101A <sup>1</sup>	3.00
Sepigel 305 <sup>2</sup>	2.50
Q2-1403 <sup>3</sup>	2.00
Isopropyl Isostearate	1.33
Arlatone 2121 <sup>4</sup>	1.00
Cetyl Alcohol CO-1695	0.72
SEFA Cottonate <sup>5</sup>	0.67
Tocopherol Acetate	0.50
Panthenol	0.50
Stearyl Alcohol	0.48
Titanium Dioxide	0.40
Disodium EDTA	0.10
Glydant Plus <sup>6</sup>	0.10
PEG-100 Stearate	0.10
Stearic Acid	0.10
Purified Water	Balance

<sup>1</sup> Isohexadecane, Presperse Inc., South Plainfield, NJ

<sup>2</sup> Polyacrylamide (and) C13-14 Isoparaffin (and) Laureth-7,

5 Seppic Corporation, Fairfield, NJ

<sup>3</sup> dimethicone (and) dimethiconol, Dow Corning Corp. Midland,  
MI

<sup>4</sup> Sorbitan Monostearate and Sucrococoate, ICI Americas Inc.,  
Wilmington, DE

10 <sup>5</sup> Sucrose ester of fatty acid

<sup>6</sup> DMDM Hydantoin (and) Iodopropynyl Butylcarbamate, Lonza  
Inc., Fairlawn, NJ

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Example 4

Illustrative of a powdered cosmetic composition according to the present invention is the formula of Table VI.

5

TABLE VI

INGREDIENT	WEIGHT %
Polysilicone-11	22.5
Cyclomethicone	59
Petrolatum	11
Ammonium Malonate (50% in water)	7
Dimethicone Copolyol	0.5

Example 5

10

A relatively anhydrous composition according to the present invention is reported in Table VII.

TABLE VII

INGREDIENT	WEIGHT %
Cyclomethicone	80.65
Dimethicone	9.60
Squalane	6.00
Isostearic Acid	1.90
Borage Seed Oil	0.90
Ammonium Malonate (50% in water)	0.50
Retinyl Palmitate	0.25
Ceramide 6	0.10
Tocopherol	0.10

15

Example 6

An aerosol packaged foaming cleanser suitable for the present invention is outlined in Table VIII.

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TABLE VIII

INGREDIENT	WEIGHT %
Sunflower Seed Oil	20.00
Maleated Soybean Oil	5.00
Silicone Urethane	1.00
Polyglycero-4 Oleate	1.00
Sodium C14-16 Olefin Sulfonate	15.00
Sodium Lauryl Ether Sulphate (25% active)	15.00
Cocoamidopropylbetaine	15.00
DC 1784® (Silicone Emulsion 50%)	5.00
Polyquaternium-11	1.00
Ammonium Malonate	1.00
Water	Balance

An aerosol is prepared using 92% by weight of the  
 5 concentrate in Table VIII and 8% propellant, the latter  
 being a combination of dimethylether, isobutane and propane.

#### Example 7

10 An adhesive cosmetic patch may also be formulated according  
 to the present invention. An adhesive hydrogel is prepared  
 by mixing 30 grams of 2-acrylamido-2-methylpropane sulphonic  
 acid monomer in 20 grams distilled water and 5 grams of a 1%  
 aqueous solution of methylene-bis-acrylamide. The solution  
 15 is then activated with 0.4% magnesium persulphate catalyst.  
 Shortly after mixing the catalyst with the hydrogel  
 solution, 0.1 grams ammonium malonate in 5ml water is added.  
 The resultant solution is coated onto a 50/50 blend of  
 polypropylene and hydrophilic polyester and allowed to  
 20 solidify. The resulting deposited hydrogel is warmed for 24  
 hours at 40°C in a hot air oven. Final water content of the  
 hydrogel is 50%. A polystyrene backing layer is laid over  
 the adhesive hydrogel.

Example 8

A disposable, single use personal towelette product is described according to the present invention. A 70/30 polyester/rayon non-woven towelette is prepared with a weight of 1.8 grams and dimensions of 15 cm by 20 cm. Onto this towelette is impregnated a composition as outlined in Table IX below.

TABLE IX

INGREDIENT	WEIGHT %
Ammonium Malonate	7.50
Glycerin	2.00
Hexylene Glycol	2.00
Disodium Capryl Amphodiacetate	1.00
Gluconolactone	0.90
Silicone Microemulsion	0.85
Witch Hazel	0.50
PEG-40 Hydrogenated Castor Oil	0.50
Fragrance	0.20
Vitamin E Acetate	0.001
Water	Balance

The foregoing description and examples illustrate selected embodiments of the present invention. In light thereof variations and modifications will be suggested to one skilled in the art, all of which are within the spirit and purview of this invention.



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CLAIMS

1. A cosmetic composition comprising:
  - (i) from about 0.0001% to about 30% by weight of a salt  
5 which is an amine neutralized malonic acid;
  - (ii) from about 1% to about 99.9% by weight of a  
cosmetically acceptable carrier;wherein the composition has a pH ranging from about 1.8  
to 6.5.  
10
2. The composition according to claim 1 wherein the amine is  
ammonia.
3. The composition according to claim 1 or claim 2 wherein  
15 the malonic acid is present as a half neutralized and a  
fully neutralized acid in a molar ratio ranging from  
about 1000:1 to about 1:1000, respectively.
4. The composition according to claim 3 wherein the molar  
20 ratio is about 2:1 to about 1:200.
5. The composition according to any of the preceding claims  
wherein the pH ranges from about 3 to about 5.5.
- 25 6. A method for controlling signs of aging including those  
selected from the group consisting of fine lines,  
wrinkles, sagging skin, poor tone and age spots,  
comprising:  
providing a cosmetic composition comprising:  
30 (i) from about 0.0001% to about 30% by weight of a salt  
which is an amine neutralized malonic acid;

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(ii) from about 1 to about 99.9% by weight of a  
cosmetically acceptable carrier;

wherein the composition has a pH ranging from about 1.8  
to 6.5.

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/05462

A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 A61K7/48

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
IPC 7 A61K

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data, EMBASE

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 33560 A (SCHERING PLOUGH HEALTHCARE) 18 September 1997 (1997-09-18) claims 1,9-11,17-19,30,39-41 page 10-15; examples 1-4 ---	1-6
X	DATABASE EMBASE 'Online! ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL; 1979 ISHIHARA N; IKEDA M: "Effects of solvents and solutes on the percutaneous absorption of m-dinitrobenzene" Database accession no. EMB-1979259894 XP002249478 abstract --- -/--	1-5

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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- \*G\* document member of the same patent family

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## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/05462

## C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	EP 0 969 089 A (HOFFMANN LA ROCHE) 5 January 2000 (2000-01-05) claims 1,5,8,20 page 28, paragraph 107 ----	1-5
Y	PATENT ABSTRACTS OF JAPAN vol. 1998, no. 11, 30 September 1998 (1998-09-30) & JP 10 175844 A (SHISEIDO CO LTD), 30 June 1998 (1998-06-30) abstract ----	1-6
Y	WO 00 61107 A (PROCTER & GAMBLE) 19 October 2000 (2000-10-19) claims 1,17,18 page 34-36; examples 4,14 ----	1-5
Y	EP 1 090 630 A (SOKEN KK) 11 April 2001 (2001-04-11) the whole document ----	1-6
Y	EP 1 192 940 A (JOHNSON & JOHNSON CONSUMER) 3 April 2002 (2002-04-03) claims 1-10 page 2, line 21 page 3, paragraph 16 page 5-6; example 1 ----	1-6
Y	EP 0 396 857 A (MUELLER R AZUCHEMIE) 14 November 1990 (1990-11-14) claims 1-6 page 2, line 1-5 page 2, line 18-35 ----	1-6
A	US 5 643 586 A (PERRICONE NICHOLAS V) 1 July 1997 (1997-07-01) column 9, line 38 -column 10, line 2 ----	1-6
A	US 5 578 641 A (JACKSON SIMON M ET AL) 26 November 1996 (1996-11-26) column 11, line 56-61 examples 4,14 -----	1-6

Form PCT/ISA/210 (continuation of second sheet) (July 1992)

## INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/05462

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9733560	A	18-09-1997	AT 239443 T	15-05-2003
			AU 723825 B2	07-09-2000
			AU 1985797 A	01-10-1997
			CA 2248876 A1	18-09-1997
			DE 69721780 D1	12-06-2003
			EP 0914083 A1	12-05-1999
			JP 11506130 T	02-06-1999
			JP 2003176216 A	24-06-2003
			WO 9733560 A1	18-09-1997
EP 0969089	A	05-01-2000	EP 0969089 A1	05-01-2000
			AU 760737 B2	22-05-2003
			AU 3675099 A	10-02-2000
			BR 9903286 A	16-05-2000
			JP 2000053584 A	22-02-2000
			KR 2000006528 A	25-01-2000
JP 10175844	A	30-06-1998	NONE	
WO 0061107	A	19-10-2000	AU 4344600 A	14-11-2000
			CN 1346264 T	24-04-2002
			EP 1169017 A1	09-01-2002
			JP 2002540898 T	03-12-2002
			WO 0061107 A1	19-10-2000
			US 6482423 B1	19-11-2002
EP 1090630	A	11-04-2001	AU 2747199 A	27-09-1999
			CA 2323451 A1	16-09-1999
			EP 1090630 A1	11-04-2001
			CN 1292682 T	25-04-2001
			WO 9945900 A1	16-09-1999
EP 1192940	A	03-04-2002	AU 7733401 A	11-04-2002
			BR 0104389 A	21-05-2002
			CA 2357958 A1	02-04-2002
			CN 1364454 A	21-08-2002
			EP 1192940 A1	03-04-2002
			JP 2002179519 A	26-06-2002
EP 0396857	A	14-11-1990	DE 3912477 A1	18-10-1990
			EP 0396857 A1	14-11-1990
			JP 2292215 A	03-12-1990
			JP 6018775 B	16-03-1994
US 5643586	A	01-07-1997	US 5554647 A	10-09-1996
			AT 219669 T	15-07-2002
			CA 2218750 A1	31-10-1996
			DE 69622035 D1	01-08-2002
			DE 69622035 T2	14-11-2002
			DK 822812 T3	14-10-2002
			EP 0822812 A1	11-02-1998
			ES 2179189 T3	16-01-2003
			PT 822812 T	29-11-2002
			WO 9633709 A1	31-10-1996
			US 5879690 A	09-03-1999
US 5578641	A	26-11-1996	AU 684282 B2	11-12-1997
			AU 6677494 A	08-11-1994

Form PCT/ISA/210 (patent family annex) (July 1992)

# INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 03/05462

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
US 5578641	A	CA 2159201 A1	27-10-1994
		DE 69407403 D1	29-01-1998
		DE 69407403 T2	09-04-1998
		WO 9423694 A1	27-10-1994
		EP 0695167 A1	07-02-1996
		ES 2110747 T3	16-02-1998
		JP 8508742 T	17-09-1996
		NZ 265618 A	27-07-1997
		ZA 9402678 A	19-10-1995